REMARKS AND ARGUMENTS.

Claims 44 and 45 have been added. Claim 44 depends from claim 1 and claim 45 depends from claim 44. It is believed, therefore, that neither claim introduces a new issue regarding unity of invention.

New claim 44 further describes a method of preventing or treating a cardiovascular or respiratory disorder in a subject by administering an effective amount of a compound of claim 1 in combination with a conventional treatment agent. Claim 45 describes the conventional treatment agent as a calcium channel blocker. Support for these features is found in the original specification at least at the following locations:

Paragraph 105 teaches that a combination therapy of a compound described by formula I herein and conventional treatment agent may also be useful for decreasing the required number of separate dosages, thus, potentially improving patient compliance. This shows that the formula I compound can be used with a separate conventional treatment agent.

Paragraph 100 teaches that "[a]s used herein, the terms "conventional treatment agent" or conventional treatment agents" refer to any compound that is other than a compound described according to formula I and is either already known or is later discovered to have efficacy for the prevention and/or treatment of a cardiovascular and/or a respiratory disorder." And paragraph 10 teaches that, "[c]urrently, vasodilators, together with CCBs [calcium channel blockers] and angiotensin inhibitors, are the accepted choice as first line medicaments for controlling blood pressure.

Accordingly, every element of the new claims is found in the specification as originally filed.

Claim 36 has been amended by adding the description of specific compounds that are useful for preventing or treating a cardiovascular or respiratory disorder.

As provided in the Rules, replacement pages for the claims are attached hereto.

Claims 1 – 45 are in the case.

No new matter has been added.

Finding that claims 1 – 35 and 37 – 43 lack inventive step over Johnson *et al., J. Pharmaceutical Sciences, 68(8)*:955-958 (1979).

The Written Opinion dated 04 April 2005, states that claims 1 – 35 and 37 – 43 lack an inventive step over the Johnson *et al.* reference, because the Applicant claims pyrrole compounds and Johnson *et al.* teaches pyrrole compounds that are structurally similar (for example chemical homologues (methyl vs. hydrogen)). The International Searching Authority then argues that a skilled practitioner would know to prepare homologues of the compounds described in Johnson *et al.* with the expectation of obtaining compounds useful in the pharmaceutical arts. The Authority concludes that compounds described in the present claims would have been suggested, and therefore they lack an inventive step.

In paragraph [00024] of the present specification, the teachings of the Johnson *et al.* reference were specifically discussed. There, it was pointed out that the 2-aminopyrrole analogs of lidocaine that were reported in the Johnson *et al.* article had been synthesized while searching for better local anesthetic and antiarrhythemic agents. Unlike any of the presently claimed compounds, the Johnson *et al.* compounds were diethyl substituted at the tertiary amine and hydrido substituted at the methyl group preceding the tertiary amine. Therefore, there is no overlap between the compounds described in the Johnson *et al.* reference and the presently claimed compounds. Furthermore, the Applicant maintains that the Johnson *et al.* article fails to provide any suggestion or motivation to produce the presently claimed compounds, or to expect that they would be successful in the claimed methods of use.

In fact, data of the antiarrhythmic activity of the eight compounds tested by Johnson *et al.* (Table IV of Johnson *et al.*) indicate that for all combinations of dosage and drug tested, over one half of the tests indicated lack of protection. Furthermore, the Johnson *et al.* reference

provides no guidance at all regarding the effect of the chemical structure of the analogues on antiarrhythmic activity. It is maintained, therefore, that the Johnson *et al.* reference would not have given a skilled practitioner a reasonable expectation that an analogue of the Johnson *et al.* compounds would have been successful for the treatment of arrythemias.

Furthermore, the publication failed to disclose methods for preventing and/or treating hypertension and asthma, and failed to teach or suggest the utility of the compounds for modulating the activity of a phosphodiesterase enzyme or an L-type calcium channel, as claimed in the present methods.

Accordingly, it is maintained that the Johnson *et al.* reference fails not only to remove the novelty of the presently claimed compounds and methods, but also it fails to provide sufficient guidance or motivation to a skilled practitioner to search for related compounds that do provide such activity. It is respectfully requested, therefore, that the finding of lack of inventive step for the present claims be reconsidered for the reasons discussed above and be withdrawn.

Respectfully submitted,

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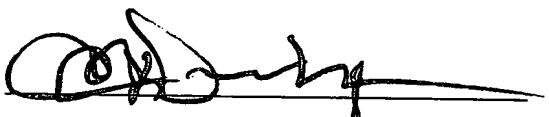

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